

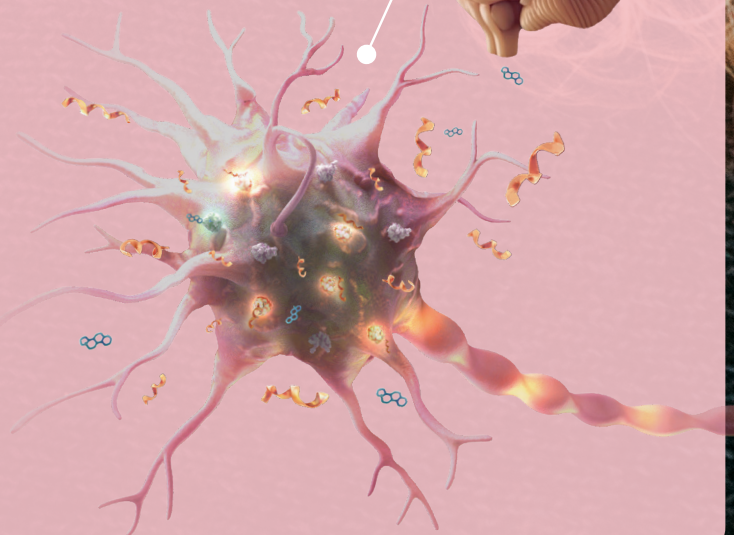
NEURONAL INFLUENCE IN MENOPAUSAL VASOMOTOR SYMPTOMS

Natural menopause is a physiologic event and an important stage of a woman's life. Up to 80% of women will experience vasomotor symptoms (VMS) due to menopause, commonly known as hot flashes and night sweats.^{1,2}

INSIDE THE SOURCE OF A HOT FLUSH

Thermoregulatory homeostasis is altered upon oestrogen decline

- 1** Inside the thermoregulatory centre in the hypothalamus, specific neurons, known as kisspeptin/neurokinin B/ dynorphin (KNDy) neurons, contribute to regulation of the body's temperature.^{3,4} These neurons are activated by the neuropeptide NKB and inhibited by oestrogen in a delicate balance.^{4,5}
- 2** Through the menopausal transition, declining oestrogen disrupts the balance with NKB. Unopposed, NKB signalling increases KNDy neuronal activity—leading to hypertrophy of the KNDy neuron and altered activity on the thermoregulatory centre.^{4,6}
- 3** As a result, the thermoregulatory centre triggers heat dissipation effectors that are experienced as hot flashes and night sweats, or VMS.^{4,6}



References: **1.** Santoro NF. Menopause. In: Crandall CJ, Bachman GA, Faubion SS, et al., eds. Menopause Practice: A Clinician's Guide. 6th ed. Pepper Pike, OH: The North American Menopause Society, 2019:1-21. **2.** Thurston RC. Vasomotor symptoms. In: Crandall CJ, Bachman GA, Faubion SS, et al., eds. Menopause Practice: A Clinician's Guide. 6th ed. Pepper Pike, OH: The North American Menopause Society, 2019:43-55. **3.** Mittelman-Smith MA, Williams H, Krajewski-Hall SJ, et al. Role for kisspeptin/neurokinin B/dynorphin (KNDy) neurons in cutaneous vasodilation and the estrogen modulation of body temperature. *Proc Natl Acad Sci U S A* 2012;109(48):19846-51. **4.** Padilla SL, Johnson CW, Barker FD, et al. A neural circuit underlying the generation of hot flashes. *Cell Rep* 2018;24(2):271-277. **5.** Krajewski-Hall SJ, Blackmore EM, McMinn JR, Rance NE. Estradiol alters body temperature regulation in the female mouse. *Temperature* 2018;5(1):56-69. **6.** Krajewski-Hall SJ, Miranda Dos Santos F, McMullen NT, et al. Glutamatergic neurokinin 3 receptor neurons in the median preoptic nucleus modulate heat-defense pathways in female mice. *Endocrinology* 2019;160(4):803-816.